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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/840,105	05/06/2004	Uwe Heinelt	DEA V2003/0047US NP	7287
5487	7590	07/12/2007		
ROSS J. OEHLER SANOFI-AVENTIS U.S. LLC 1041 ROUTE 202-206 MAIL CODE: D303A BRIDGEWATER, NJ 08807			EXAMINER LOEWE, SUN JAE Y	
			ART UNIT 1626	PAPER NUMBER
			NOTIFICATION DATE 07/12/2007	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/840,105	Applicant(s) HEINELT ET AL.	
	Examiner Sun Jae Y. Loewe	Art Unit 1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5-9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-3 and 5-9 are pending in the instant application. Claim 4 was cancelled by amendment filed on May 30, 2007.

Response to Amendment

2. The amendment filed was fully considered, however, it does not overcome the 35 USC 103 rejection set forth in the previous office action.

Response to Arguments

3. Applicant's arguments filed on May 30, 2007 have been fully considered but they are not persuasive for the following reasons.

Applicants state that the references of Kim et al. in combination with those of Lee et al. and Williams et al. do not disclose nor suggest that an efficient cyclization can take place with $X=NR^5$ or sulfur. Applicants further state that the cyclization reaction is sensitive to changes in the starting materials and reaction conditions, thus one of ordinary skill could not predict where the TsCl reacts when $X=NR^5$ or sulfur.

The reference of Kim et al., as well as that of Lee et al., show that the reaction with TsCl leads to the formation of the o-cyclization product (ie. the carbodiimide intermediate) provided that the reactive site is $-NR^3 = -NH$ – see Table 1 for Kim et al. or Table 1/Scheme 2 for Lee et al. Furthermore, the reference of Williams et al. expressly suggests the use of nitrogen as a nucleophile in reactions with carbodiimides. Thus, the combination of the three references does suggest using with $X=NR^5$ in the cyclization reaction (ie. cyclodesulfurization).

The 35 USC 103 rejection previously made discusses these points in further detail. For clarity, the rejection is reiterated below.

Claim Rejections - USC § 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

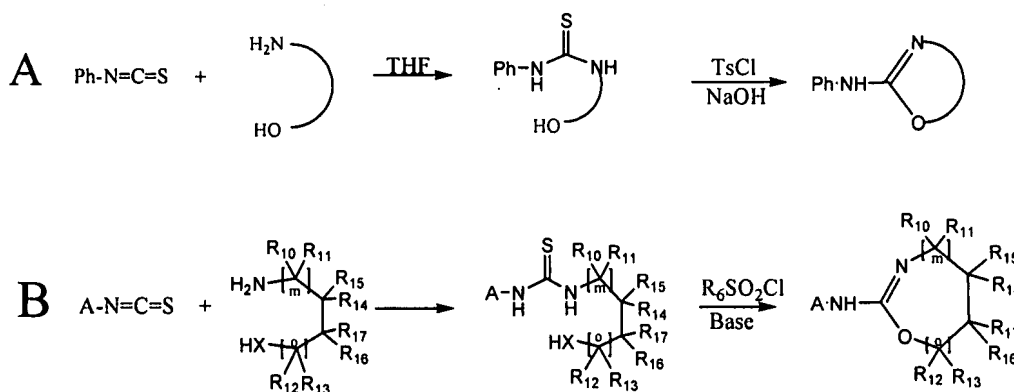
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
 2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
4. Claims 1-3, 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. *Tetrahedron Lett.* (2001), 42, 2413.

Scheme 1. Comparison of Reactions in Kim et al. (A) and Instant Claims (B)

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Determination of the scope and contents of the prior art.

Kim et al. teach the cyclodesulfurization of N-(2-hydroxyethyl)-N'-phenylthioureas using p-toluenesulfonyl chloride and NaOH (Scheme 1A). N-(2-hydroxyethyl)-N'-phenylthiourea is prepared by reacting phenyl isothiocyanate with a 1,2-aminoalcohol.

Ascertaining the differences between the prior art and the claims at issue.

The instant claims are directed the cyclodesulfurization of thioureas, formed by reacting isothiocyanates with amino alcohols, amino mercaptans and diamines, which lead to the formation of heterocycles of variable ring size (Scheme 1B), see claim 1. Both the formation of thiourea and subsequent cyclodesulfurization is taught in the prior art.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.

The instant invention wherein X=O is the same process taught by Kim et al, merely using alternate compounds with the same reactive sites. A multitude of starting materials, that would lead to heterocycles of variable ring size and that would fall into the scope of the claimed invention, are available commercially. One skilled in the art in possession of the reference and such alternate starting materials would be motivated to practice the claimed invention with reasonable expectation of success. See for example *In re Surrey et al* (CCPS 1963) 319 F2d 233, 138 USPQ 67 (the mere use of different starting materials in a conventional process to produce the product one would expect therefrom does not render the process unobvious).

5. Claims 1-3, 5-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al.

Tetrahedron Lett. (2001), 42, 2413 in view Lee et al *Bull. Korean Chem. Soc.* 2002, 23, p.19-20

and Williams et al. *Chem. Rev.* 1981, 81, 589-636.

Determination of the scope and contents of the prior art.

Kim et al. teach the cyclodesulfurization of N-(2-hydroxyethyl)-N'-phenylthioureas using p-toluenesulfonyl chloride and NaOH (Scheme 1A). N-(2-hydroxyethyl)-N'-phenylthiourea is prepared by reacting phenyl isothiocyanate with a 1,2-aminoalcohol.

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Lee et al. teach that the cyclodesulfurization of N-(2-hydroxyethyl)-N'-phenylthioureas to form oxazoline derivatives (process disclosed by Kim et al) proceeds via initial formation of a carbodiimide intermediate, and subsequent attack of the carbodiimide carbon by the OH nucleophile. Finally, Williams et al (p. 600) teach reactions of carbodiimides involving nitrogen nucleophiles.

Ascertaining the differences between the prior art and the claims at issue.

See above, paragraph 4.

The use of $X=NR_5$ is not taught by the primary reference of Kim et al.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.

See above, paragraph 4.

It is well known in the art that any species with an unshared pair of electrons (ie. Lewis base) can be used as a nucleophile. Moreover, Williams et al expressly suggests the use of nitrogen as a nucleophile in reactions of carbodiimide (p. 600), which is the pathway for cyclodesulfurization taught by Lee et al. Many primary amines which contain the NR_5 functionality and fall into the scope of the claimed invention are available commercially (for instance, 1,3-diamino propane, cysteamine, cadaverine). One with ordinary skill in the art in possession of the references and the starting materials would be motivated to practice the claimed invention with reasonable expectation of success. See for example Mills et al. v Watson, Comr. Pats (CADC 1955) 223 F2d 335, 105 USPQ 355 (use of a known member of a class of materials in a process is not patentable if other members of the class were known to be useful for that purpose).

Conclusion

6. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

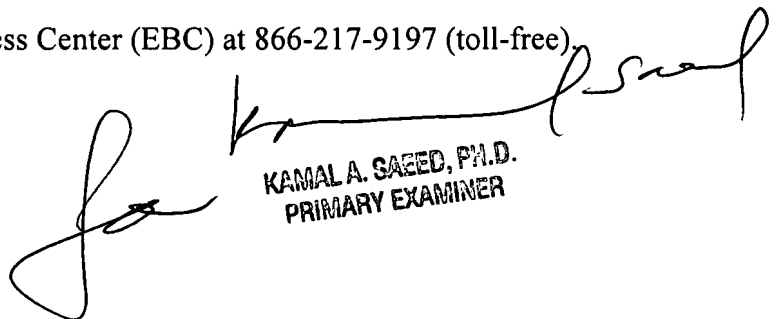
however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication should be directed to Sun Jae Y. Loewe, whose telephone number is 571-272-9074. The examiner can normally be reached on Monday through Friday from 7:30 am to 5:00 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Cecilia Tsang (571) 272-0562, can be reached. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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PRIMARY EXAMINER